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D E C I S I O N
of 29 April 1997

Case Number: T 0413/94 - 3.3.4

Application Number: 85306827.8

Publication Number: 0183350

IPC: C12N 15/27

Language of the proceedings: EN

Title of invention:
DNA Encoding human colony stimulating factor, peptide encoded thereby, vectors and transformed hosts containing such DNA, and the production of all thereof

Patentee:
IMMUNEX CORPORATION

Opponent:
Novartis AG Patent and Trademark Dept.

Headword:
Human CM-CSF/IMMUNEX CORP.

Relevant legal provisions:
EPC Art. 56, 87

Keyword:
"First priority - (no) - not same invention"
"Inventive step - (no)"

Decisions cited:
T 0073/88, T0081/87

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0413/94 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 29 April 1997

Appellant: (Proprietor of the patent)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 25 March 1994 revoking European patent No. 0 183 350 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: F. L. Davison-Brunel
S. C. Perryman

Summary of Facts and Submissions

I. European patent No. 0 183 350 with the title "DNA encoding human colony stimulating factor, peptide encoded thereby, vectors and transformed hosts containing such DNA, and the production of all thereof" was granted with seven claims based on European application No. 85 306 827.8 claiming priority from US 666041 (29 October 1984) and US 750401 (2 July 1985).

Claim 1 read as follows:

"A recombinant DNA expression vector comprising a promoter that directs expression in a yeast host of a recombinant DNA coding sequence which:

(a) encodes a mature human granulocyte macrophage colony stimulating factor (GM-CSF) protein having N-terminal alanine-proline residues, which protein is capable of stimulating growth of human bone marrow colonies in the human bone marrow colony assay;

(b) hybridizes to a radiolabeled single-stranded DNA probe consisting of a PstI-Hae III fragment of the murine GM-CSF gene corresponding to nucleotides 45 through 400 indicated in Figure 1, after overnight hybridization in 6xSSC at 55°C followed by washing with 6xSSC; and

(c) is fused at its 5' terminus to a leader sequence derived from a yeast mating pheromone gene that directs secretion of said mature human GM-CSF protein into culture medium upon cleavage of such leader from said N-terminal alanine- proline residues."

Claims 2 to 4 further related to specific embodiments of the recombinant expression vector of claim 1. Claim 5 related to the specific vector deposited as ATCC 53157. Claim 6 was directed to a yeast host cell transformed with the recombinant DNA expression vector according to any of the preceding claims and claim 7 was directed to the use of the yeast host according to claim 6 to produce mature, human GM-CSF.

Corresponding process claims were granted for AT.

II. A notice of opposition was filed requesting the revocation of the patent under Article 100(a) EPC (lack of inventive step) and under Article 100(b) EPC (insufficiency of disclosure). The later request under Article 100(b) EPC was withdrawn during the course of the proceedings.

The documents cited during opposition proceedings which were considered most relevant by the Opposition Division are the following:

(2): Wong et al., Science, 17 May 1985, volume 228, pages 810 to 815;

(3): Brake et al., Proc.Natl.Acad.Sci., 1984, volume 81, pages 4642 to 4646;

(4): Bitter et al., Proc.Natl.Acad.Sci., 1984, volume 81, pages 5330 to 5334;

(5): Singh et al., Nucl.Ac.Res., 1984, volume 12, pages 8927 to 8938.

III. By a decision within the meaning of Article 102(1) EPC dated 25 March 1994, the Opposition Division revoked the patent for lack of inventive step.

It was decided that the claims could only enjoy priority rights from 2 July 1985.

The closest prior art was, thus, identified as document (2) published on 17 May 1985, which provided the sequence of the GM-CSF gene and described its transient expression in monkey COS cells. The combination of this document with any of the documents (3) to (5) which disclosed the expression and secretion of foreign proteins from yeast expression-secretion vectors was found to negatively affect inventive step.

IV. The Appellant (Patentee) lodged an appeal against the decision of the Opposition Division and filed the statement of grounds of appeal.

V. The Respondent (Opponent) answered to the Appellant's submission.

VI. A communication was sent by the Board according to Article 11(2) EPC of the Rules of procedure of the Boards of Appeal setting out the Board's preliminary position.

VII. Oral proceedings were held on 29 April 1997.

VIII. The submissions in writing and during oral proceedings by the Appellant can be summarized as follows:

In accordance with the case law of the EPO, T 0073/88 (OJ EPO 92, 557), the patent was entitled to the first priority date as the added feature (c) in claim 1 simply was a specific embodiment of a vector useful in the general production system (i.e. recombinant DNA technology) disclosed in the first priority application. Furthermore, feature (c) did not relate to

the character and nature of the invention which was the provision of the sequence of human GM-CSF and feature (c) was not at all essential for the real contribution to the invention.

The situation was unlike that encountered in T 0081/87 (OJ EPO 90, 250) where priority was denied for a claim to the production of pre-prorennin from a priority application which neither disclosed the sequence of pre-prorennin nor disclosed a clone containing the full pre-prorennin DNA sequence. In the present case the sequence of the GM-CSF DNA was part of the first priority application. The invention claimed was the provision of the GM-CSF DNA and this was disclosed in the first priority application. The features of the claims not specifically disclosed in the first priority application could be ignored when assessing the identity of the invention, and thus did not make the invention claimed different from that disclosed in the first priority application.

Document (2), which described the cloning and expression in COS cells of the GM-CSF DNA, was published only between the dates of filing of the first priority and the second priority. While if it were held by the Board that the claims of the patent in suit were only entitled to the second priority date, document (2) would be state of the art for the purpose of assessing inventive step, it was not so citable because the claims were entitled to the date of filing of the first priority application.

IX. The Respondent replied as follows:

The claims of the patent could not be entitled to priority from the first priority application. They were directed to the expression of human GM-CSF DNA into yeast whereas the priority application was solely concerned with the cloning and sequencing of human GM-CSF.

The conclusions reached in T 0073/88 (cf. supra) were not of any relevance to the present situation as this earlier decision dealt with a case where the feature added in the claim 1 of the European patent amounted to a limitation of a generic teaching found in the priority application. Here, on the contrary, the specific expression vector in claim 1 of the patent in suit did not constitute a limitation from a general disclosure in the priority application, since expression vectors were not mentioned in said application at all. Rather the claim was directed to a different invention from that disclosed in the first priority application.

The added feature (c) was clearly an essential feature of the invention as claimed. The situation, thus, was comparable to that encountered in T 0081/87 (cf. supra) as in this earlier case an essential element, the sequence of the pre-prorennin DNA, was also missing from the priority application.

Document (2) was thus part of the state of the art, and also was the closest prior art. It described the cloning and expression in COS cells of the GM-CSF DNA. Documents (3) to (5) gave unequivocal evidence that, at the second priority date, yeast vectors with the yeast alpha-factor leader sequence had been successfully used

for the expression of mammalian proteins. The combination of document (2) with any of documents (3) to (5) rendered obvious the subject-matter of claim 1.

IX. The Appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the claims as granted.

X. The Respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible

Priority (Articles 87 and 88 EPC)

2. The invention as claimed in claim 1 is a yeast recombinant expression vector comprising such regulatory elements as a promoter and the leader sequence of a yeast mating pheromone gene (feature 1 (c)). On the other hand, the first priority application discloses the cloning of human GM-CSF DNA into E.coli plasmid **cloning** vectors. The possibility of **cloning** in yeast plasmids vectors is also envisaged. However, **expression** of the GM-CSF DNA is not contemplated in any hosts. Yeast expression vectors are not mentioned at all, let alone expression vectors with feature 1 (c).

3. Thus the Board concludes that the subject-matter of claim 1, namely a recombinant vector for expression of GM-CSF in yeasts, is not the same invention as that disclosed in the first priority application, namely the cloning of the GM-CSF gene.

4. It was argued by the Appellant that the only feature of claim 1 which did not appear in the priority application was feature (c) and that this feature did not alter the nature of the invention. Therefore, according to the case law of the EPO (T 0073/88, see supra), priority should be acknowledged.

5. The Board cannot agree with this argument. In T 0073/88 (cf. supra), the conclusion was reached that "In a case where a feature in a claim is not related to the function and effect of the invention, such feature is not related to the character and nature of the invention, and the absence of such a feature does not cause loss of priority provided the claim is otherwise in substance in respect of the same invention in the priority application". In the present case, however, the claim is not in substance in respect of the same invention as in the priority application (see point 3, above). Thus, T 0073/88 (cf. supra) is not relevant.

6. Since the first priority application and claim 1 do not relate to the same invention, claim 1 is not pursuant to Article 87(1) EPC entitled to the date of filing, 29 October 1984, of the first priority application.

7. The second priority application discloses the same invention as the European patent in suit: the expression of human GM-CSF DNA in yeast from a yeast recombinant expression vector comprising a promoter and the yeast alpha-factor leader sequence. Priority can, thus, be acknowledged from 2 July 1985, the date of filing of the second priority application. However document (2) was published before this, on 17 May 1985, and so is part of the state of the art.

Inventive step (Article 56 EPC)

8. Both parties agree that if the claims are only entitled to priority from 2 July 1985, document (2) published on 17 May 1985 which discloses the cloning and expression in COS cells of the GM-CSF DNA is to be considered as closest prior art. The Board also shares this opinion.

9. Starting from this prior art, the objective problem to be solved can be defined as the stable production of human GM-CSF in large quantities.

10. The solution provided is to express GM-CSF DNA in yeast cells from a yeast expression-secretion vector.

11. Each of documents (3) to (5) describes the expression and secretion of human proteins in yeasts, excretion being directed by the yeast alpha-factor leader sequence. Document (4), in particular, suggests the fusion between the yeast alpha-factor leader sequence and the DNA sequence of any mature foreign protein as a means to easily retrieve large quantities of the mature protein in the culture medium. In the Board's view, the combination of the teachings of document (2) and any of documents (3) to (5) leads in a straightforward manner to the proposed solution.

12. It does not appear, nor was it argued by the Appellant, that any technical skill above that of the average skilled person would have been required to put into practice the above obvious solution derived from the prior art.

13. For these reasons, the Board is of the opinion that no inventive step is involved in the subject-matter of claim 1.

14. The Board, thus, concludes that the requirement of Article 56 EPC is not fulfilled.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

A. Townend U. Kinkeldey

Beglaubigt/Certified Certifiée conforme: München/Munich
Geschäftsstelle Registry/Greffe
10. JUNI 1997